

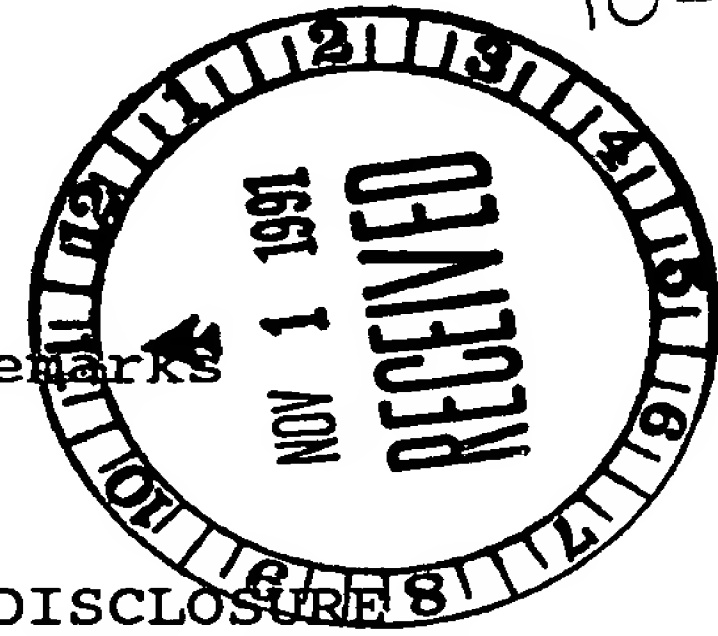
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PATENT
PC6947A/6970AGCB

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: : EXAMINER: E. Peselev
Stephen P. Gibson et al. : ART UNIT: 183
SERIAL NO.: 07/142,888 : BATCH NO.: R90 18X
FILED: January 11, 1988 :
ALLOWED: August 7, 1991 :
FOR: ANTIPARASITIC AGENTS :
(AS AMENDED) :

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231



SUPPLEMENTAL INFORMATION DISCLOSURE
STATEMENT UNDER 37 C.F.R. §§1.98 and 1.99

Sir:

Pursuant to Applicants' duty of disclosure, Applicants cite the following additional references which are also listed on the enclosed form PTO-FB-A820 (2 pages). Copies of the references also are enclosed.

While prosecution of the application has ended, Applicants respectfully request that the Examiner fully consider the additional references cited herein as the additional references were cited by an opponent in opposition to grant of a patent from a European patent application which is the counterpart of the instant application. The notice of opposition from the European Patent Office with copies of the cited references was sent to Pfizer Limited, a subsidiary of the assignee of this application, on October 11, 1991. The notice was received by Pfizer Limited on October 14, 1991 and a copy thereof with the cited references was received by the undersigned on October 17, 1991.

A copy of the Notice of Opposition from the European Patent Office is attached hereto. As the references cited below have, in addition to certain of the references already of record, been cited in opposition to grant of a patent from the counterpart European application, it is believed that the additional references are material.

Applicants wish to thank the Examiner for the telephone interview held on October 30, 1991 during which Applicants' undersigned representative informed the Examiner of Applicants' desire to have the additional references considered and made of record. Pursuant to that interview, Applicants hereby provide the Examiner with this Supplemental Information Disclosure Statement and copies of the references, and respectfully request that the Examiner fully consider the additional references cited herein.

Jpn 58-78594 discloses, inter alia, a process for producing higher yields of certain milbemycin compounds having an isopropyl group at C-25 by adding to a culture of certain Streptomyces one or more of valine, isobutyric acid, isovaleric acid, 2-ketoisovaleric acid, isocaproic acid, a salt or ester thereof, or isobutanol or its ester.

Derwent Abstract, Accession No. 84-01600, appears to correspond to the reference of Chen, S. T., et al., Abstr. Pap. Am. Chem. Soc. (1983) 186 Meet., MBTD 28 already of record. The abstract discloses, inter alia, that the C-25 moieties of avermectins a and b derive from 2-methylbutyrate and isobutyrate, respectively.

Cane, D. E., et al., disclose, inter alia, that L-isoleucine is a precursor of the starter unit for avermectins having a sec-butyl group at C-25.

Kaneda, T., Can. J. Microbiol. 12:501-504 (1966) discloses, inter alia, that synthesis by Bacillus subtilis of certain fatty acids is increased by adding L-isoleucine, L-leucine, L-valine, α -methylbutyrate, isovalerate or isobutyrate to a certain medium through a synthesis mechanism which includes acyl-CoA esters.

Dreher, R. et al. disclose, inter alia, a mutant of Bacillus subtilis which synthesizes ω -cyclopropane, ω -cyclobutane, ω -cyclopentane, ω -cyclohexane and ω -cyclohexen fatty acids when fed the respective alicyclic carboxylic acids.

Kaneda, T., Biochem. Biophys. Res. Comm. 99:1226-1229 (1981) discloses, inter alia, that a certain strain of

Bacillus subtilis incorporates 2-(±)-cyclopentenecarboxylic acid into certain cyclopentenyl fatty acids when added to the culture medium.

Oshima, M. et al. disclose, inter alia, the existence of certain ω-cyclohexyl fatty acids in certain thermophilic bacteria and the synthesis thereof from glucose.

Poralla, K. et al. disclose, inter alia, certain ω-cycloheptane fatty acids in new species of thermo-acidophilic Bacillus.

DeRosa, M. et al. disclose, inter alia, the effects on synthesis of certain fatty acids by Bacillus acidocaldarius when various precursors are added to the culture.

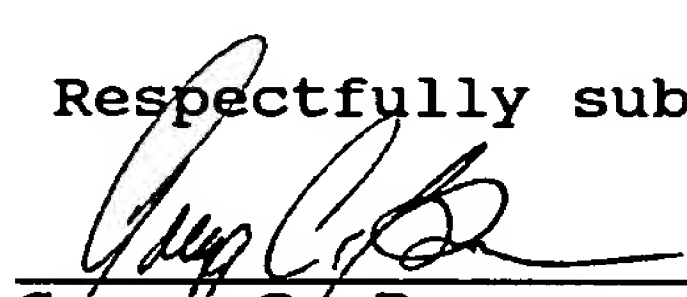
The Examiner is requested to consider carefully the complete text of these references in connection with the examination of the above-identified application in accord with 37 CFR 1.104(a). It is believed the Examiner will concur with Applicants' belief that the subject matter presently claimed is neither anticipated nor rendered obvious by the foregoing references.

It is requested that the references listed on the attached form PTO-FB-A820 be included in the "References Cited" portion of any patent issuing from this application (M.P.E.P. 1302.12).

A prompt and favorable response is earnestly solicited.

Date: October 31, 1991

Respectfully submitted,



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